Amendments to the Specification:

Please replace paragraph [0003] of the published application with the following amended paragraph:

Alzheimer's Disease (AD) represents one of the great unsolved medical needs confronting society during this millennium. Despite considerable work during the past quarter century, no medicines exist that attack the underlying pathophysiology of the disease. One of the cardinal features of AD is deposition of plaques comprised of aggregated beta-amyloid peptides (Aβ) in the brain, particularly in regions associated with cognition and memory. Selkoe, *Annu. Rev. Neurosci.*, 17, 489-517 (1994). Overproduction of Aβ, which appears to be directly neurotoxic, can be detected at the earliest stages of AD and, in fact, before cognitive dysfunction is detectable. [[AD]]Aβ is produced from its precursor protein, APP, by proteolytic processing at its N and C termini by β- and γ-secretase enzymes, respectively. Mutations in APP, presenilin-1, or presenilin-2 genes result in over-production of Aβ1-42 peptide and cause early onset, familial AD. The identity of the β- and γ-secretases have been studied since 1984, and in 1999 the elusive N-terminal β-site APP cleaving enzyme (BACE-1) was reported. Yan, *et al.*, *Nature*, 402, 533-537 (1999). It remains possible that there are additional proteases with [[≠]]β-secretase activity.

Please replace paragraph [0046] of the published application with the following amended paragraph:

Some transgenic animals of the invention have both an inactivation of one or both alleles of BACE-1 and a second transgene that confers an additional phenotype related to Alzheimer's,

disease, its pathology or underlying biochemical processes. For example, some transgenic animals have an inactivation of one or both alleles of BACE-1 and a second transgene encoding a variant form of APP, in which the variation is associated with familial Alzheimer's disease. Such animals can be produced by breeding a transgenic animal with a functional inactivation of BACE-1 with a transgenic animal expressing a mutated form of human APP. Examples of the latter include mice bearing a 717 mutation of APP described by Games *et al.*, [[supra]] *Nature* 373, 523-527, and mice bearing a Swedish mutation of APP such as described by McConlogue *et al.*, US 5,612,486 and Hsiao *et al.*, *Science* 274, 99 (1996); Staufenbiel *et al.*, *Proc. Natl. Acad. Sci. USA* 94, 13287-13292 (1997); Sturchler-Pierrat *et al.*, *Proc. Natl. Acad. Sci. USA* 94, 13287-13292 (1997); Borchelt *et al.*, *Neuron* 19, 939-945 (1997)). The 717 mutation of APP can be phenylalanine, glycine or isoleucine.